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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/700,333

11/03/2003

Mark Ledebner

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VERTEX PHARMACEUTICALS INC.  
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EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

ART UNIT

PAPER NUMBER

1624

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

03/21/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/700,333	<b>Applicant(s)</b> LEDEBOER ET AL.	
	<b>Examiner</b> Venkataraman Balasubramanian	<b>Art Unit</b> 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 21 December 2006.  
 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.  
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,5-29,31,32,34,35,37,38 and 40-58 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
 6) ☒ Claim(s) 1,5-29,31,32,34,35,37,38 and 40-58 is/are rejected.  
 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) ☐ All b) ☐ Some \* c) ☐ None of:  
 1. ☐ Certified copies of the priority documents have been received.  
 2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: _____  |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :12/21/2006, 7/25/2006, 7/3/2006.

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### **DETAILED ACTION**

Applicants' response, which included cancellation of claims 4, 59 and amendment to claims 1, 5, 45, 46 and 56-58, filed on 12/21/2006, is made of record. Claims 1, 5-29, 31, 32, 34, 35, 37, 38 and 40-58 are now pending. In view of applicants' response, all 112 rejections and prior art 102 and 103 rejections made in the previous office have been obviated. However, the following rejections apply to currently pending claims.

#### ***Information Disclosure Statement***

References cited in the Information Disclosure Statement field on 12/21/2006, 7/3/2006 & 7/25/2006 are made of record.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 57 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting JAK kinase activity in a standard biological assay, does not reasonably provide enablement for a method of inhibiting JAK kinase activity in a biological sample generally for the purpose of blood

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transfusion, organ transplantation, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claim is drawn to 'a method of inhibiting JAK kinase activity in a biological sample' and the term "biological sample" as per the definition in the specification (page 65 "includes, without limitation, cell cultures or extracts thereof; biopsied material obtained from a mammal or extracts thereof; and blood, saliva, urine, feces, semen, tears, or other body fluids or extracts thereof").

First, the instant claim 57 is a 'reach through' claim. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through to the corresponding therapeutic method of any or all diseases, disorders or conditions, for which they lack written description and enabling

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disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention.

As can be seen from the definition of the term "biological sample", without limitation it reads on many and all types of biological samples, which can include mammals or animals and therefore, the claimed method is seen to encompass an inhibitory method wherein the compound is administered to an animal. This is further evident from the purpose of the inhibition of JAK kinase activity stated in page 74, paragraph 00212, which includes for example, blood transfusion, organ-transplantation, etc. As the inhibition of JAK kinase activity in a biological sample is disclosed to be useful for blood transfusion, organ-transplantation, etc., it implicitly reads on the inherent therapeutic methods characterized by the activity, which as per the specification includes numerous types of diseases/disorders recited in pages 70-74.

The sole testing assay provided in the specification at pages 83-85 is to test the ability of the compounds to inhibit JAK kinase activity using a standard enzyme system, however, there is insufficient guidance in the disclosure regarding the provided assay. Next, applicant has not provided how this correlates with the efficacy in all types of biological samples encompassed by the instant method and their use in the various purposes wherein the inhibition activity is useful. For example, blood transfusion is the process of transferring blood or blood-based products from one person into the circulatory system of another. Blood transfusions may be seen as a procedure to treat some medical conditions, such as massive blood loss due to trauma, surgery, shock and where the red cell producing mechanism (or some other normal and essential

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component) fails. Similarly, an organ transplantation is the transplantation of a whole or partial organ from one body to another (or from a donor site on the patient's own body), for the purpose of replacing the recipient's damaged or failing organ with a working one from the donor site. As can be seen from the above, without limitation these purposes are intended for therapeutic methods and applicant has not provided competent evidence sufficient to enable the claimed method.

Further, the originally claimed method alternatively recited the use of 'a pharmaceutical composition comprising the compound of formula I and a pharmaceutically acceptable carrier, adjuvant or vehicle' as being added to the biological sample, see the last three lines of the claim. A pharmaceutical composition of the kind recited in the instant claims is generally used for internal administration type therapeutic methods. Therefore, the instant claim appears to be directed to the various types of therapeutic methods associated with JAK kinase inhibition activity.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the

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time the application was 'filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The claimed invention lacks patentable utility. As noted above in the 112 first paragraph rejection, the method of inhibiting JAK kinase activity is implicitly intended for treating various diseases. However, as recited in the amended claims appear to be for inhibiting the said enzyme in biological samples. Specification does not teach or suggest any utility of the instant compounds. Hence, the method of inhibiting JAK kinase activity lacks utility to the extent it is limited to inhibition of JAK kinase in biological samples.

Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions for which they lack written description and enabling disclosure in the specification.

In the instant case, because of the interaction of the compound formula I with various kinases, it is recited that instant compounds are useful for treating or lessening the severity of any or all disorders and diseases selected from a proliferative disorder, a



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cardiac disorder, a neurogenerative disorder, a psychotic disorder, an autoimmune disorder, a condition associated with organ transplant, an inflammatory disorder, an immunologically mediated disorder, viral disease, or a bone disorder for which there is no adequate written description and enabling disclosure in the instant specification.

As can be seen from the definition of the term "biological sample" stated in page 65 of specification, without limitation it reads on many and all types of biological samples, which can include mammals or animals and therefore, the claimed method is seen to encompass an inhibitory method wherein the compound is administered to an animal. This is further evident from the purpose of the inhibition of various kinases activity stated in specification at various places for treating various diseases. As the inhibition of kinases in a biological sample is disclosed to be useful, it implicitly reads on the inherent therapeutic methods characterized by the activity, which as per the specification includes numerous types of diseases/disorders recited in specification pages 70-74. Therefore, the instant claim appears to be directed to the various types of therapeutic methods.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

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F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5-29, 31, 32, 34, 35, 37, 38 and 40-58, provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5-22 and 24 of copending Application No. 10/702,113. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of instant claims namely compound, composition and method of use substantially overlap with claims 1, 5-22 and 24 of the copending application. See formula I of instant claims and formula I of the copending application and note the overlap of various variable groups. Thus, it would have been obvious to one trained in the art at the time of the invention to select any of the species of the genus taught by the reference including those compounds claimed in the instant invention and expect the resultant compound to possess the use taught in the reference in view of equivalency of various compounds generically taught with those exemplified therein.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 5-29, 31, 32, 34, 35, 37, 38 and 40-58, provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over

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claims 1-60 of copending Application No. 10/639,784. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of instant claims namely compound, composition and method of use substantially overlap with claims 1-60 of the copending application. See formula I of instant claim 1 and formula I of the copending application and note the overlap of various variable groups. Thus, it would have been obvious to one trained in the art at the time of the invention to select any of the species of the genus taught by the reference including those compounds claimed in the instant invention and expect the resultant compound to possess the use taught in the reference in view of equivalency of various compounds generically taught with those exemplified therein.

### **Conclusion**

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status

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information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

  
Venkataraman Balasubramanian

3/19/2007